Established in 1871

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Review article: Biomedical intelligence | Published 27 December 2017 | doi:10.4414/smw.2017.14566
Cite this as: Swiss Med Wkly. 2017;147:w14566

Treatment of dizziness: an interdisciplinary update

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Summary

This review provides an update on interdisciplinary treatment for dizziness. Dizziness can have various causes and the treatment offered should depend on the cause. After reading this article, the clinician will have an overview of current treatment recommendations. Recommendations are made for the most prevalent causes of dizziness including acute and chronic vestibular syndromes, vestibular neuritis, benign paroxysmal positional vertigo, endolymphatic hydrops and Menière's disease, vestibular paroxysmia and vestibular migraine, cardiac causes, transient ischaemic attacks and strokes, episodic ataxia type 2, persistent postural-perceptual dizziness, bilateral vestibulopathy, degenerative, autoimmune and neoplastic diseases, upbeat- and downbeat nystagmus. Recommendations include clinical approaches (repositioning manoeuvres), medication (adding, removing or changing current medication depending on aetiology), vestibular physiotherapy, ergotherapy and rehabilitation, treatment of chest pain or stroke units and operative interventions. If symptoms are acute and severe, medication with antivertigo agents is recommended as a first step, for a maximum period of 3 days. Following initial symptom control, treatment is tailored depending on aetiology. To assist the clinician in obtaining a useful overview, the level of evidence and number needed to treat are reported whenever possible based on study characteristics. In addition, warnings about possible arrhythmias due to medications are issued, and precautions to enable these to be avoided are discussed.

Key words: *dizziness, emergency, vertigo, vestibular, HINTS*

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Introduction

This review summarises treatment approaches for different types of vestibular syndromes with central and peripheral aetiologies. It relates to prior reviews [1–3] and adds recent developments in the field. It also complements the manuscript on diagnostic procedures for dizziness in the emergency department published in this journal [4]. Where no studies exist, tentative recommendations based on clinical expertise are made. This review aims at providing an overview of currently available treatment strategies for clinicians of different disciplines. Even though specialist consultation might still be required, knowledge about current treatment options facilitates interdisciplinary dialogue.

Acute vestibular syndrome

An acute vestibular syndrome consists of an acute onset of dizziness associated with nystagmus, nausea, light-headedness and balance problems and lasting longer than 24 hours [5, 6]. In almost any acute vestibular syndrome, the following symptomatic treatment can be prescribed for the first 3 days: an antihistamine such as dimenhydrinate orally 50 mg every 4–6 hours or as a suppository 150 mg once or twice per 24 hours [1], an anticholinergic such as transdermal scopolamine 1 mg every 72 hours [1], a benzodiazepine such as diazepam orally 5–10 mg every 4–6 hours, or clonazepam orally 0.5 mg every 4–8 hours [1, 3]. Such medications should, however, not be taken for more than 3 days, because they are believed to inhibit central compensatory processes, and benzodiazepines have addictive potential [1]. The evidence for recommending these three medications for symptomatic treatment is rather weak. It is based on expert opinion. On the other hand, experts have observed thousands of patients in the German Dizziness Center. For the future, it is necessary to perform prospective, comparative studies that permit the calculation of a number needed to treat.

Before prescribing dimenhydrinate, an electrocardiogram (ECG) should be recorded. A second ECG should be recorded after initiating treatment with dimenhydrinate, because it can cause a prolongation of the frequency corrected QT interval. Consequently, there is the danger of the Torsade-de-pointes arrhythmia, especially if the patient has

a congenital or acquired long QTc interval, is also taking other potentially QTc prolonging drugs in addition to dimenhydrinate, or has other risk factors such as low serum potassium levels. No absolute risk numbers can be provided, though, because patients with long QTc syndrome are excluded from studies with QTc-prolonging agents. To avoid putting patients at risk, we recommend an ECG. It is particularly important to avoid combining QTc-prolonging drugs. Instead, treatment alternatives should be considered. It is noteworthy that benzodiazepines themselves can be the cause of dizziness. Moreover, the combination of different benzodiazepines is discouraged. Antihistamines, anticholinergics and benzodiazepines are also referred to as antivertiginosa [1]. Prior to prescribing them, however, the primary care physician can try to alleviate the symptoms by other means. For example, if the patient suffers from benign paroxysmal positional vertigo, a repositioning manoeuvre is indicated. Examples of how to carry out this manoeuvre are described in this review. If the primary care physician cannot manage the symptoms, antivertigonosa can be applied to treat acute episodes of dizziness [1]. Although we are not aware of comparative trials that make exact reference to the number of days for which they should be administered, we suggest a prescription over a maximum of 3 days in the recommended doses of dimenhydrinate, scopolamine and clonazepam [1, 3]. Although the aim must be to refer the patient to the specialist as fast as possible if treatment attempts by the emergency physician fail, not all patients get an immediate appointment. In such a case, antivertigonosa are a good choice to control the symptoms. Once the patient has seen the specialist, the right diagnosis can be made and the treatment with antivertigonosa can be stopped in favour of another treatment.

Acute unilateral vestibulopathy

An acute vestibular syndrome in which drug therapy might be useful is acute unilateral vestibulopathy [1–3, 7–9]. A detailed overview of the symptoms of acute vestibular syndrome is described in the accompanying article on diagnosis [4]. Dizziness is often linked to an oscillating visual perception (oscillopsia), nausea, postural instability and ataxia. The cause may be re-activation of herpes simplex virus type 1 in the vestibular ganglia [1–3, 8, 9], although there is no definite proof for this hypothesis [1–3].

To control acute symptoms, antivertiginosa [1–3, 8] can be applied as described above. If the cochlea or the vestibulocochlear nerves are involved (also known as labyrinthitis), this condition can be associated with hearing loss. In this case, the patient should be referred to an ear, nose and throat specialist. The vestibular nerve lies in a bony canal and nerve ischaemia due to inflammation-related swelling can be reduced by administration of methylprednisolone; thereby vestibular function may recover [1–3, 10–13]. The level of evidence in these studies ranges from 1 [12] to 3 [11, 13]. The number needed to treat ranges between two and three in all three studies for corticosteroid treatment versus no treatment. Note that one study [12] had no no-treatment group, so the exact number needed to treat can only be estimated from other studies on how many patients without treatment have spontaneous remission. It is noteworthy that a 6-month follow-up showed no superiority of corticosteroids over physical therapy [12], with even a slight advantage for physical therapy over corticosteroid treatment (level of evidence 1, number needed to treat 20). Methylprednisolone should be administered in a daily oral dose of 100 mg and this dose should be reduced by 20 mg every fourth day [1–3]. Alternatively, prednisolone can be administered. During treatment, patients' blood sugar levels should be monitored. The risk for gastric ulcers should be considered. If the patient has a risk factor for gastric ulcers and if there is co-medication with non-steroidal anti-inflammatory drugs or a high bleeding risk due to platelet inhibitors or a therapeutic anticoagulation regimen in addition to cortisone, the administration of a proton pump inhibitor should be considered. We also recommend that patients at risk for osteoporosis receive a calcium and vitamin D supplement, such as 1000 mg of calcium and 800 IU of vitamin D daily.

There is evidence that physiotherapy, which can foster central vestibular compensatory mechanisms [1–3], additionally helps to control symptoms and is at least, if not more effective, than corticosteroid treatment [12]. In particular, there is evidence for significant symptom reduction following vestibular physiotherapy [8, 12, 14–21]. Vestibular physiotherapy can help to train balance in uni- or bilateral peripheral aetiologies or in visual vertigo [14–18]. Therefore, physiotherapy should be initiated at first presentation. We consider physiotherapy to be at least as important as pharmacotherapy. It is, however, necessary that the patient sees a physiotherapist who is specialised in vestibular physiotherapy. Depending on the healthcare system, it may be necessary to explicitly mention vestibular physiotherapy on the prescription.

Stroke

Acute vestibular syndrome can also be caused by central aetiologies, with cerebellar stroke being the most common central cause [22].

Cerebellar stroke can mimic the signs of peripheral vestibulopathy. Downbeat nystagmus is present in about 50% of cerebellar strokes [22, 23]. Consequently, a cerebellar infarction should always be considered as a differential diagnosis, even if peripheral vestibulopathic failure is suspected [22]. As in brainstem strokes, gaze-evoked nystagmus is a sensitive sign of a lesion within the cerebellum [22, 24]. If recognised within the appropriate timeframe and after exclusion of contraindications, thrombolysis is indicated. Therefore, a neurologist should be involved if stroke remains among differential diagnoses during initial evaluation. If indicated, an intravenous or intra-arterial thrombolytic agent should be administered within the first 4.5 [1] to 6 hours [25]. Intravenous thrombolysis consists of systemic administration of recombinant tissue plasminogen activator to re-perfuse thrombotic occlusions. Intra-arterial thrombolysis requires a catheter to be placed near the thrombotic occlusion, with the aim of achieving thrombolysis at the location of the blocked artery. Studies and recommendations on thrombolysis, however, are subject to continuous re-evaluation. There are cases where patients benefit from thrombolysis even beyond 6 hours after symptom onset. It is noteworthy that some patients often have no symptoms other than dizziness, nystagmus and imbalance [22]. For this reason, it is important to recognise the symptoms and to correctly classify them as central rather than peripheral causes. Even if no stroke is present, audio and vestibular loss can reflect a significant steno-

sis of the anterior inferior cerebellar artery [22, 26, 27] and precede an imminent stroke [22, 26, 27]. Patients with isolated hearing loss or dizziness may have a labyrinthine stroke, as the inner ear receives its blood supply from the vertebrobasilar system [22]. Labyrinthine stroke or stenosis of the internal auditory artery may not be recognised with magnetic resonance imaging (MRI) [22]. Given that approximately 20% of strokes are within the vertebrobasilar circulation, isolated vertigo due to labyrinthine stroke is not unusual. Whenever a significant stenosis is suspected, for example because of repeated transient ischaemic attacks, an analysis of the blood vessels with either computed tomography (CT) or MRI angiography is mandatory [22, 28–30]. On one hand, it is important to recognise present or imminent stroke to reduce the damage resulting from ischaemia; on the other hand this treatment might itself result in harmful consequences [31–33]. If a transient ischaemic attack or stroke is recognised, the start of treatment was linked to an 80% risk reduction of additional disability due to a subsequent stroke [31]. This does not mean that all patients need thrombolysis, but it means that the transient ischaemic attack or stroke is recognised and treatment is initiated, for example by beginning treatment with platelet inhibitors, oral anticoagulants or a statin [32]. In order to recognise significant stenoses, CT- or MR-angiography is necessary and patients should be referred to centres where it is available. Harmful consequences and risks of diagnostic tests and treatment, such as contrast-induced nephropathy, need to be considered. Not all patients will be candidates for systemic thrombolysis, for example patients with isolated vertigo, which results in a zero value in the National Institutes of Health Stroke Scale. The risk of systemic thrombolysis includes potentially fatal intracranial haemorrhages, which occur in 2% of patients within the first couple of days after its application [33]. As an initial guide as to whether the patient suffers from a stroke, several clinical tests have proved useful. They are described in our accompanying manuscript on diagnosis and elsewhere [4, 5, 22, 34–37].

Episodic vestibular syndromes

An episodic vestibular syndrome is defined as dizziness lasting less than 24 hours. Consequently, it may consist of a short episode or repeated short episodes. It can be associated with nausea, balance problems, nystagmus or motion intolerance [38]. A prominent example of an episodic vestibular syndrome is benign paroxysmal positional vertigo, which will be described in the next section.

Benign paroxysmal positional vertigo and repositioning manoeuvres

The most important therapeutic procedures to treat benign paroxysmal positional vertigo, where otolithic debris is moving inside a canal (canalolithiasis) [3, 39–43] or inside/near the cupula (cupulolithiasis) [39, 44–46], are repositioning manoeuvres. The majority of benign paroxysmal positional vertigo is idiopathic. Known causal factors include ototoxic medication [47], prolonged bed rest [48], cervical hyperextension [49], osteoporosis [50, 51], age [52], and migraine [53]. There are prospects for treatments and prophylaxis of some of these conditions, such as osteoporosis and migraine.

There are four types of benign paroxysmal positional vertigo, depending on the involvement of a specific semicircular canal. Diagnostic manoeuvres to identify the affected canal are summarised in table 1, repositioning manoeuvres in figure 1. The most commonly involved semicircular canals are the posterior ones [65] (90%). Note that repositioning manoeuvres should be performed by trained individuals, since an incorrectly applied manoeuvre might induce an iatrogenic switch or conversion of the affected canal, for example from a posterior benign paroxysmal positional vertigo to a horizontal benign paroxysmal positional vertigo [66–68]. Otolith repositioning should only be performed after determination of the affected canal by means of diagnostic positioning techniques. A detailed overview of other individual manoeuvres can be found in the literature [54]. In addition, figures 1A and 1B show the correct head and body positions during repositioning manoeuvres of the posterior semicircular canal.

Endolymphatic hydrops and Menière's disease

Among the different episodic vestibular syndromes, Menière's disease has been extensively studied [1–3, 69–98]. It is characterised by recurrent attacks of dizziness, hearing loss and the sensation of ear pressure, as well as tinnitus, probably due to an endolymph hydrops (overproduction or under-resorption of endolymph) [1–3, 86, 87]. As a result, there is recurrent leakage through the membrane separating endolymph and perilymph spaces [1–3]. Hence, the therapeutic goal is to reduce the production or to enhance the absorption of endolymph [1–3]. The degree of individual suffering can sometimes appear alarming when the patient first presents to medical staff [92]. So far, there are more than 6000 articles on Menière's disease. Articles cover a wide spectrum of therapeutic recommendations [1–3, 69–91, 93–98]. The treatment of Menière's disease consists of several steps depending on the stage and severity of disease [69]. The therapeutic goal is to reduce the number of attacks in order to prevent future vestibular deficits [69]. Conservative treatments include salt restriction or the administration of diuretics [1–3,

Table 1: Benign paroxysmal positional vertigo, the affected semicircular canal, and the repositioning manoeuvre.

Affected semicircular canal	**Repositioning manoeuvre** [3, 42–44, 46, 54, 55]
Posterior (Barany 1921 [56])	Epley [57] Semont [58]
Horizontal geotropic (Mac Clure 1985 [59])	Barbecue, Gufoni for geotropic form [43, 60]
Horizontal apogeotropic (Baloh et al. 1995 [61])	Gufoni for ageotropic form [42]
Anterior (Bertholon et al. [62], Califano et al. 2014 [63])	Canalith repositioning technique (CRT) [64]

Note: A geotropic nystagmus beats towards the earth, ageotropic nystagmus beats in the opposite direction. Videos for illustration purposes are provided online at https://smw.ch/en/article/doi/smw.2017.14566/.

69–71, 89]. Whereas some authors recommend that therapy can be initiated with salt restriction followed by diuretics [69], others doubt the benefits of this treatment approach and warn of potentially harmful consequences [70, 71] of salt restriction or diuretics. In our opinion, this approach is not recommended. Other conservative treatments include the administration of an H_1-agonist/H_3-antagonist (betahistine dihydrochloride) or its metabolites [69, 72–76, 88–91]. Betahistine dihydrochloride improves microcirculation in the inner ear, resulting in better balance between endolymph production and resorption [1, 2, 73–75, 88]. Although a recently published long-term, multicentre, double blind, randomised, placebo-controlled study did not find evidence for successful symptom control with betahistine dihydrochloride [72], other results, including data from a meta-analysis [76], suggest symptom control after betahistine dihydrochloride administration [1–3, 76, 89–91]. Based on clinical experience with 112 patients over a period of 12 months, it is recommended to administer 48 mg betahistine dihydrochloride orally three times daily [1–3, 90]. In individual cases, this dose can be increased up to 480 mg daily if no sufficient symptom alleviation is achieved after 3 months of treatment [1, 91].

As a second step, more invasive treatments, such as intratympanic steroid injections, may be considered [1, 2, 77, 78, 93–96]. Such treatments, although invasive, still have low complication rates and minimal side effects [1, 2]. Intratympanic instillations of 0.4–1 ml high-dose dexamethasone solution (12 mg/ml) [95] might also be effective, though not as effective as gentamycin instillation [1, 2, 96]. Double-blind, placebo-controlled trials demonstrated symptom reduction following intratympanic steroid injection [78, 93]. In contrast to an aminoglycoside instillation (see third step below), however, it is not associated with hearing loss [1, 2, 77, 78, 93–96].

As a third step, more invasive options are reserved for patients with intractable Menière's disease. Chemoablative agents, such as gentamicin, proved successful in reducing the attacks of Menière's disease [1–3, 79, 81, 82, 87, 98]. Its obvious downside is possible hearing loss [97], which is the reason why it is recommended in patients with preexisting hearing loss. New protocols with low-dose fractioned transtympanic application of gentamicin (diluted gentamicin, 26.7 mg/ml, pH 6.4, weekly for 4 weeks) aim to reduce the risk of hearing loss [83, 87, 98]. Gentamicin damages the hair cells responsible for vestibular information in the inner ear [80]. Hence, its prophylactic administration is associated with a decrease of attacks. It can also cause hearing loss owing to the proximity of other hair cells responsible for hearing. Surgical approaches are also discussed in the literature [86]. Patients with hearing loss might benefit from labyrinthectomy, whereas patients with preserved hearing are candidates for selective vestibular neurectomy with hearing preservation [99]. Other surgical procedures such as endolymphatic sac surgery are not recommended owing to lack of evidence of beneficial effects [86].

be repeated several times.

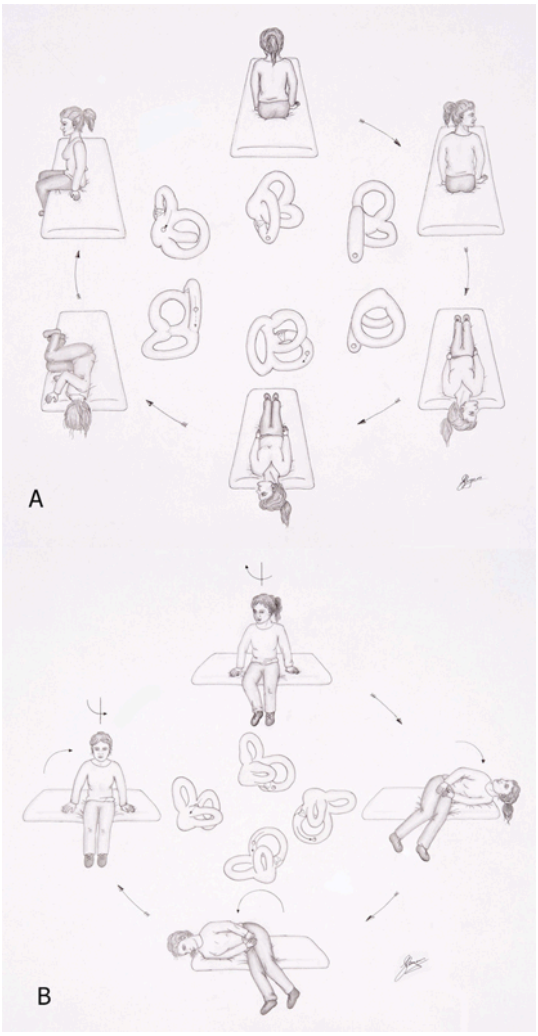

Figure 1: Two examples of repositioning manoeuvres for benign paroxysmal positional vertigo (BPPV) due to an affected posterior semicircular canal.(A) The Epley manoeuvre. The patient sits on the examination table, slightly off centre to the end of the table. The head is turned 45° to the affected side. The patient is pushed backwards in a lying position with the head hanging over the end of the table in a brisk movement. This manoeuvre will cause dizziness and the patient should be warned beforehand. When the dizziness stops the head is slowly turned to the other side facing first the ceiling, then the other wall of the room and finally – also turning the body in the direction of the head – the floor. Compliance of and communication with the patient is essential to prevent back injuries. The turning movement should be performed slowly, taking into account the slowly moving stones and the high viscosity in the semicircular canal. The patient will suffer from another episode of dizziness when the head is turned away from the affected side. When the dizziness ceases the patient is pushed upright into a sitting position. The last movement should be led by the doctor because sitting on the side of the bed will again produce an episode of dizziness.(B) The Semont manoeuvre. The patient is seated opposite the doctor. The head is turned 45° away from the affected side. The upper body of the patient is pulled sideways leaving the head in the turned position. The patient is put in a half-lying position looking upward to the ceiling. The patient should be warned beforehand that this positioning can cause dizziness. The patient is held in this position for more than 1 minute until the dizziness stops, then pulled in the opposite direction with a brisk movement, to the other side of the bed, lying on the shoulder of the unaffected side with the head facing the floor. The patient is held in this position for the same time that as in the first position. Finally, the patient is put again in the seated, primary position. The Semont manoeuvre is a good alternative to the Epley manoeuvre for patients with back problems. Nevertheless, the back and the neck of the patient should be protected at all times. The manoeuvre can

In summary, the more invasive methods such as gentamicin treatment or neurectomy are more effective, but are also associated with risks and adverse effects. We recommend starting with the least invasive methods mentioned in step 1 and slowly progressing to more invasive options if the severity of symptoms cannot be controlled otherwise. In any case, it is necessary to inform the patient about the risks and to make sure that invasive procedures are carried out by clinicians with the relevant experience. If the patient cannot be examined by a specialist immediately, clinicians without expertise regarding Menière's disease should consider administering antivertiginosa or betahistine dihydrochloride. Subsequently, the clinicians should make sure that the patient is seen by a specialist.

Superior canal dehiscence syndrome

Superior canal dehiscence syndrome is an episodic vestibular syndrome [100–104]. It consists of dizziness combined with auditory symptoms such autophony, hyperacusis and tinnitus induced by sound or pressure. The reason for this pressure transmission is a bony dehiscence of the superior semicircular canal, first described by Minor in 1998 [101]. Surgical repair such as capping, re-surfacing or plugging of the superior semicircular canal is recommended [102–104].

Vestibular paroxysmia

Drug therapy may alleviate symptoms of vestibular paroxysmia [1, 2], which is recurrent attacks of spinning vertigo persisting up to 1 minute [1, 2]. Vestibular paroxysmia may rarely be accompanied by either tinnitus or decreased hearing [1]. It often leads to unsteadiness of stance or gait and can be provoked by a change in head position or by hyperventilation [1, 105, 106]. Its origin is probably a compression of the eighth cranial nerve by blood vessels near the brainstem [1, 2, 105–108]. Recommended medications are oral carbamazepine 200–600 mg per day [1, 2, 106], in some cases up to 800 mg per day [1], or oxcarbazepine in slightly higher doses. The efficacy of oxcarbazepine to relieve symptoms was demonstrated in a group of patients who received a mean dose of 870 mg of per day [106]. For both carbamazepine and oxcarbazepine, we recommend starting with a low dose and progressing slowly to higher doses. The weakness of these recommendations is that prospective, randomised, comparative trials do not exist. Therefore, a number needed to treat cannot be computed. The following recommendations in this section rely on expert opinion (level of evidence 5). Consequently, prospective studies with comparative treatment arms are strongly encouraged.

If carbamazepine is not tolerated, there are alternatives, such as phenytoin, gabapentin or valproate, although these are not based on evidence [1, 2]. Patients therefore need to be informed of the off-label administration. We would also recommend looking for potential side-effects and contraindications, such as high-level atrioventricular block, bradycardia, electrolyte imbalances, etc. In our opinion, treatment should start with low doses: for example, in adults 100 mg phenytoin orally once daily, which can be subsequently increased up to three times per day (over the next four to six days, increasing the dose every two to three days). With gabapentin, the starting dose could be 300 mg once on day one, to be increased to twice daily on day two and three times daily on day three. Only if it shows partial yet insufficient symptom relief would we recommend a further increase. Because this is off-label use and empirical evidence is lacking, we would not recommend a daily dose higher than 1800 mg. Valproate dosing, on the other hand, is more dependent on body weight. We would start with 10 mg per kilogram body weight, and increase the dose every three days to a maximum daily dose of 20 mg per kilogram body weight. Antiepileptic medications can themselves elicit dizziness [109, 110], so they should be administered cautiously. We would also recommend that they are prescribed only by a specialist who is able to differentiate possible side effects from the sensation of dizziness *per se* and who carries out the necessary laboratory checks. In particular, valproate can be associated with blood count changes such as leucopenia and thrombopenia or elevated liver enzymes.

Vestibular migraine

Another episodic vestibular syndrome of central origin is vestibular migraine. It is characterised by attacks of either dizziness alone or with stance and gait ataxia, headache, nausea, vomiting and visual sensations [1–3]. These episodes might last minutes to hours and can be first treated symptomatically with the previously mentioned antivertigonosa [1]. For the future, prospective, placebo-controlled clinical studies analysing vestibular migraine are needed. The principles of migraine treatment can be applied to prevent attacks of vestibular migraine. We recommend prophylactic oral administration of topiramate 25–100 mg daily or valproate 300–900 mg daily [1, 111] or the sustained release form of metoprolol 50–200 mg daily [1, 112, 113]. There was no clear evidence for the benefits of zolmitriptan in vestibular migraine [113, 114], whereas slightly better effects were found for the prophylactic oral administration of propranolol 40–240 mg daily [113, 115], amitriptyline 50–100 mg daily [113, 116], flunarizine 5–10 mg daily [112, 113], and acetazolamide 250–750 mg daily [113, 117]. If the patient takes several medications, it is necessary to check for drug-drug interactions and to consider the QTc prolonging effect (see Introduction).

Cardiac causes and transient ischaemic attacks

Cardiac problems cause orthostatic dizziness, which can be treated with compression stockings, but the majority of cardiac causes identified in a systematic review were actually true vertigo [118]. Hence, whenever patients report the sensation of dizziness, it is important to remember that this could have a cardiovascular, valvular or arrhythmic origin. In some cases, patients may benefit from revascularisation, valve repair/replacement or antiarrhythmic treatment. If atrial fibrillation has persisted for more than 48 hours, cardioversion into sinus rhythm should be attempted only after exclusion of an atrial thrombus by transoesophageal echocardiography.

As mentioned previously, stroke is also a potential cause of dizziness. The same holds true for transient ischaemic attacks, where patients may have isolated dizziness or other stroke symptoms for less than 24 hours and without acute ischaemic lesions on MRI. In addition, intermittent isolated vertigo may also be caused by vertebrobasilar insufficiency preceding a stroke [22, 26]. Patients who suffer a transient ischaemic attack should undergo neurovascular

ultrasonography to look for plaques or stenoses, echocardiography, and a long-term ECG to look for atrial fibrillation (if atrial fibrillation was not already present in the ECG upon admission) [119]. Treatment of transient ischaemic attacks is a statin and aspirin [119]. The most recent stroke prevention guidelines should be consulted [119] and vascular risk factors should be sought. If the patient is on a factor Xa inhibitor for atrial fibrillation and suffers from a transient ischaemic attack, anti-factor Xa activity should be determined as a therapy check. If the medication has insufficient effect, anticoagulant treatment should be changed. If the transient ischaemic attack occurs under previously established statin treatment, switching to another statin should be considered, because, apart from lipid levels, the plaque-stabilising effects of statins might differ. Thromboendarterectomy or stenting should be considered in the case of symptomatic stenoses such as subclavian artery stenosis or the rare cases of symptomatic carotid stenosis associated with dizziness [119].

Episodic ataxia type 2

There are a number of inherited syndromes with recurrent attacks of dizziness and ataxia [1–3, 120, 121]. Among these inherited syndromes, episodic ataxia type 2 is the most frequent [1]. Symptoms are dizziness and ataxia of several hours duration, which are often elicited by physical activity, alcohol consumption or stress [1–3]. Over 90% of the patients have oculomotor disorders such as downbeat nystagmus [1]. Successful treatment approaches include the administration of an aminopyridine [122–124]. Current recommendations include the off-label oral administration of 5 mg 4-aminopyridine three times daily [1, 2, 122] or the off-label oral administration of 10 mg of the sustained release form dalfampridine once or twice daily [1, 2, 123, 124].

Persisting vestibular syndromes

A chronic vestibular syndrome is a combination of symptoms with persistent dizziness lasting months to years and other symptoms such as oscillopsia, nystagmus and gait disturbance. They include persistent postural-perceptual dizziness, bilateral vestibulopathic failure, degenerative, autoimmune or neoplastic diseases, vestibular syndromes with downbeat or upbeat nystagmus, and dizziness due to isolated causes. Examples of the different chronic vestibular syndromes will be provided in the following sections.

Persistent postural-perceptual dizziness

Persistent postural-perceptual dizziness is an umbrella term for known psychosomatic disorders such as secondary somatoform dizziness or phobic positional vertigo. Phobic positional vertigo can be treated with vestibular physiotherapy and cognitive behavioural therapy, possibly combined with antidepressants such as selective serotonin reuptake inhibitors [1, 3], for example citalopram 10–20 mg per day [1]. If selective serotonin reuptake inhibitors are not sufficient, it is also possible to try serotonin norepinephrine reuptake inhibitors [125, 126]. It is necessary to record an ECG prior to the initiation of and during treatment with the antidepressant. In addition, it is necessary to check the serum electrolytes, as many antidepressants can be associated with low sodium levels.

Bilateral vestibulopathy

Bilateral vestibulopathy is characterised by postural imbalance, gait impairment and, in some patients, oscillopsia [127]. Its major cause is the administration of aminoglycosides such as gentamicin or streptomycin [127, 128]. Aminoglycosides are often used to treat severe infections such as endocarditis. Other causes of bilateral vestibulopathy are chemotherapy with cisplatin [127, 129] and autoimmune inner ear disease, which usually affects both vestibular function and hearing [127] and may also have ocular manifestations when parts of the peripheral or central nervous system involving the eye are affected. Examples are autoimmune or infectious inflammatory processes, neoplasms, traumas or malformations. Typical ocular effects happen during a probably autoimmune inflammation of the cornea as in Cogan's syndrome [127, 130]. Other pathological mechanisms include bacterial or viral meningitis [127], bilateral vestibular neuritis [127, 131, 132], bilateral vestibular Schwannomas [127], bilateral Menière disease [127, 133], neurosyphilis/neurolues [127, 134, 135], neurosarcoidosis [127, 136], congenital malformations [127] or head trauma [127, 137, 138]. It can be recognised in the emergency department, at the bedside or in the outpatient setting by comparing visual acuity during head rotation with visual acuity when the head is still [127, 139, 140].

The underlying causes of bilateral vestibular loss need to be eliminated or symptomatically treated, for example by stopping aminoglycosides whenever possible. In general, patients should be informed about possible side-effects prior to starting treatment with aminoglycosides, so that they can directly report to the clinician if these symptoms start. If the full picture of vestibulopathy has developed, it mostly persists, because destroyed hair cells in the inner ear do not regenerate [127] and only the future will show whether molecular gene transfer approaches that work in the mouse model will provide symptom relief in humans [141]. Hence, the best approach is to stop the medication when signs of vestibulopathy first develop, as some hair cells may still be saved this way. In persisting bilateral vestibular loss, the main approach to date is vestibular rehabilitation by means of physiotherapy [16–18, 127, 142]. We recommend that physiotherapy is provided by an expert specialised in vestibular loss.

Degenerative, autoimmune and neoplastic diseases

It is necessary to apply anti-inflammatory treatment for inflammatory lesions and autoimmune diseases [1], with high-dose glucocorticoid treatment or other immunosuppressive or immune-modulating drugs [1].

Neurologists should be consulted if there is evidence for an inflammatory lesion. Similarly, these lesions may be caused by tumours or be the result of post-ischaemic events. It is necessary to keep in mind that the symptoms can be the same irrespective of the original cause, with the location of the lesion determining what symptoms the patient may experience [1, 3].

Vestibular syndromes with downbeat or upbeat nystagmus

Dizziness can be associated with vertical forms of nystagmus (downbeat or upbeat nystagmus) [1–3]. Both downbeat and upbeat nystagmus usually coincide with sway

vertigo and gait ataxia [1]. They have central aetiologies, such as Arnold-Chiari malformation, cerebellar atrophy and ischaemic or inflammatory lesions in the brainstem or cerebellum, or are idiopathic [1, 143, 144]. Current recommendations include the off-label oral administration of 4-aminopyridine 5–10 mg two to three times daily in both downbeat nystagmus [1–3, 145–147] and upbeat nystagmus [1–3, 148], the oral administration of 3,4-diaminopyridine 10–20 mg two to three times daily [1–3, 149], or the oral administration of clonazepam 0.5 mg three times daily [1, 150–152]. Due to its addictive potential and the impairment of central compensation mechanisms [1], we do not recommend the administration of clonazepam for more than 3 days. If the symptoms are minor, drug treatment can even be omitted. Downbeat nystagmus will usually improve throughout the day [153], especially when the head remains in an upright position [143]. According to recent evidence from an observational study, it may be further improved by resting in darkness with the head in an upright position [154].

There are additional forms of nystagmus that go along with dizziness, but these are less frequent than downbeat or upbeat nystagmus. These less frequent forms of nystagmus, such as acquired pendular nystagmus or periodic alternating nystagmus, are not be summarised here. Detailed recent reviews and therapeutic recommendations can be found elsewhere [1, 2, 152].

Dizziness due to isolated causes

Some cases of dizziness have a clearly defined origin. These include peripheral neuropathy, for example due to deficiency of vitamin B1, B6 or B12 or to diabetes. Recommended therapy is treatment of the vitamin deficiency or better control of diabetes, in addition to physiotherapy and ergotherapy (use of supportive equipment, adapted shoes, etc.). Further isolated causes include ophthalmological aetiologies, such as a decrease in visual acuity, defects in visual fields or binocular vision, anisometropia, multifocal acuity correction or metamorphopsia and particular forms of cataract [155]. In these cases, it is vital to optimise ophthalmological treatment to reduce the sensation of dizziness. Dizziness following anaemia due to gastrointestinal blood loss requires identification of the cause and specific treatment. Another cause of dizziness is cervical vertigo [156], which could be due to degenerative vertebral processes, trauma [157] or nerve compressions. Treatment includes manual therapy, muscle relaxants or anti-inflammatory medication [156], specific vestibular rehabilitation [156, 157], and stress-reduction and anxiety-reducing techniques [157]. More details on the specific treatments are provided elsewhere [156, 157]. If there is a significant nerve compression that cannot be treated conservatively, interventional approaches remain a therapeutic option. Other isolated causes of dizziness include acute infections (which require treatment according to the infectious focus), and respiratory diseases associated with hypercapnia. When the underlying aetiology is treated successfully, the acute vestibular sensation may also disappear. Such medical conditions could include either a single cause, such as pulmonary embolism or myocardial infarction, an electrolyte imbalance, or an infection, or have multiple causes.

Conclusion

This review summarises current treatment recommendations for different forms of dizziness. Optimal treatment strategies should be tailored to the individual patient and underlying aetiology. They should involve multidisciplinary approaches including neurology, ear-nose-throat, ophthalmology, general internal medicine, emergency medicine and neurosurgery, physiotherapy and ergotherapy. In many cases, it is possible to treat the symptoms of dizziness, but not to entirely reverse the cause, for example in cerebellar stroke or bilateral vestibular loss. Many recommendations are based on retrospective cohort studies (level of evidence 3), case series (level of evidence 4) and expert recommendations or case reports (level of evidence 5), which calls for future prospective studies with higher levels of evidence. Given that dizziness is one of the most frequent reasons why patients consult general practitioners and emergency departments, it is important to stimulate future research. This would allow us to make recommendations based on higher levels of evidence. It is particularly important to have comparative studies where different treatment approaches are compared with each other and with placebo. The first steps in this direction have already taken place; for example, there is a multicentre, randomised placebo-controlled trial underway on treatment of vestibular paroxysmia (VESPA) [158]. Hopefully similar trials will be made possible for the other causes of dizziness.

Acknowledgement

The authors thank Christian Nickel for his most valuable comments.

Financial disclosure

The authors Roger Kalla and Georgios Mantokoudis were supported by the Swiss National Science Foundation (Grant #320030_173081). Raoul Sutter received research grants from the Swiss National Foundation (No 320030_169379), the Research Fund of the University of Basel, The Scientific society Basel and the Gottfried Julia Bangerter-Rhyner Foundation.

Competing interests

Raoul Sutter received personal grants from UCB-pharma and Destin Pharma GmbH and holds stocks from Novartis and Roche. Heiko Rust has received travel support from Bayer Healthcare, Teva and Genzyme.

References

1 Strupp M, Kremmyda O, Bremova T, Teufel J. Aktuelles zur Pharmakotherapie von Schwindel und Nystagmus. Arzneimitteltherapie. 2013;31:147–55. Article in German.

2 Strupp M, Kremmyda O, Brandt T. Pharmacotherapy of vestibular disorders and nystagmus. Semin Neurol. 2013;33(3):286–96. doi: http://dx.doi.org/10.1055/s-0033-1354594. PubMed.

3 Strupp M, Brandt T. Diagnosis and treatment of vertigo and dizziness. Dtsch Arztebl Int. 2008;105:173–80. PubMed.

4 Spiegel R, Kirsch M, Rosin C, Rust H, Baumann T, Sutter R, et al. Dizziness in the emergency department: an update on diagnosis. Swiss Med Wkly. 2017;147:w14565.

5 Kattah JC, Talkad AV, Wang DZ, Hsieh YH, Newman-Toker DE. HINTS to diagnose stroke in the acute vestibular syndrome: three-step bedside oculomotor examination more sensitive than early MRI diffusion-weighted imaging. Stroke. 2009;40(11):3504–10. doi: http://dx.doi.org/10.1161/STROKEAHA.109.551234. PubMed.

6 Hotson JR, Baloh RW. Acute vestibular syndrome. N Engl J Med. 1998;339(10):680–5. doi: http://dx.doi.org/10.1056/NEJM199809033391007. PubMed.

7 Strupp M, Magnusson M. Acute Unilateral Vestibulopathy. Neurol Clin. 2015;33(3):669–85, x. doi: http://dx.doi.org/10.1016/j.ncl.2015.04.012. PubMed.

8 Jeong SH, Kim HJ, Kim JS. Vestibular neuritis. Semin Neurol. 2013;33(3):185–94. doi: http://dx.doi.org/10.1055/s-0033-1354598. PubMed.

9 Arbusow V, Schulz P, Strupp M, Dieterich M, von Reinhardstoettner A, Rauch E, et al. Distribution of herpes simplex virus type 1 in human geniculate and vestibular ganglia: implications for vestibular neuritis. Ann Neurol. 1999;46(3):416–9. doi: http://dx.doi.org/10.1002/1531-8249(199909)46:3<416::AID-ANA20>3.0.CO;2-W. PubMed.

10 Strupp M, Zingler VC, Arbusow V, Niklas D, Maag KP, Dieterich M, et al. Methylprednisolone, valacyclovir, or the combination for vestibular neuritis. N Engl J Med. 2004;351(4):354–61. doi: http://dx.doi.org/10.1056/NEJMoa033280. PubMed.

11 Batuecas-Caletrío A, Yañez-Gonzalez R, Sanchez-Blanco C, Pérez PB, González-Sanchez E, Sanchez LA, et al. Glucocorticoids improve acute dizziness symptoms following acute unilateral vestibulopathy. J Neurol. 2015;262(11):2578–82. doi: http://dx.doi.org/10.1007/s00415-015-7918-x. PubMed.

12 Goudakos JK, Markou KD, Psillas G, Vital V, Tsaligopoulos M. Corticosteroids and vestibular exercises in vestibular neuritis. Single-blind randomized clinical trial. JAMA Otolaryngol Head Neck Surg. 2014;140(5):434–40. doi: http://dx.doi.org/10.1001/jamaoto.2014.48. PubMed.

13 Karlberg ML, Magnusson M. Treatment of acute vestibular neuronitis with glucocorticoids. Otol Neurotol. 2011;32(7):1140–3. doi: http://dx.doi.org/10.1097/MAO.0b013e3182267e24. PubMed.

14 Bronstein AM, Golding JF, Gresty MA. Vertigo and dizziness from environmental motion: visual vertigo, motion sickness, and drivers' disorientation. Semin Neurol. 2013;33(3):219–30. doi: http://dx.doi.org/10.1055/s-0033-1354602. PubMed.

15 Cawthorne T. The rationale of physiotherapy in vertigo and facial palsy. Physiotherapy. 1952;38(12):237–41. PubMed.

16 Black FO, Pesznecker SC. Vestibular adaptation and rehabilitation. Curr Opin Otolaryngol Head Neck Surg. 2003;11(5):355–60. doi: http://dx.doi.org/10.1097/00020840-200310000-00008. PubMed.

17 Pavlou M, Shumway-Cook A, Horak F, et al. Rehabilitation of balance disorders in the patient with vestibular pathology. In: Bronstein AM, Brandt T, Woollacott MH, Nutt JG, eds. Clinical disorders of balance and gait: Oxford University Press; 2004:211–35.

18 Bronstein A, Lempert T. Dizziness: A Practical Approach to Diagnosis and Management. Cambridge, England: Cambridge University Press; 2002.

19 Strupp M, Arbusow V, Maag KP, Gall C, Brandt T. Vestibular exercises improve central vestibulospinal compensation after vestibular neuritis. Neurology. 1998;51(3):838–44. doi: http://dx.doi.org/10.1212/WNL.51.3.838. PubMed.

20 Hillier SL, Hollohan V. Vestibular rehabilitation for unilateral peripheral vestibular dysfunction. Cochrane Database Syst Rev. 2007;(4):CD005397. PubMed.

21 Hillier SL, McDonnell M. Vestibular rehabilitation for unilateral peripheral vestibular dysfunction. Cochrane Database Syst Rev. 2011;(2):CD005397. PubMed.

22 Kim JS, Lee H. Vertigo due to posterior circulation stroke. Semin Neurol. 2013;33(3):179–84. doi: http://dx.doi.org/10.1055/s-0033-1354600. PubMed.

23 Huh YE, Kim JS. Patterns of spontaneous and head-shaking nystagmus in cerebellar infarction: imaging correlations. Brain. 2011;134(12):3662–71. doi: http://dx.doi.org/10.1093/brain/awr269. PubMed.

24 Baier B, Dieterich M. Incidence and anatomy of gaze-evoked nystagmus in patients with cerebellar lesions. Neurology. 2011;76(4):361–5. doi: http://dx.doi.org/10.1212/WNL.0b013e318208f4c3. PubMed.

25 Sandercock P, Wardlaw JM, Lindley RI, Dennis M, Cohen G, Murray G, et al., IST-3 collaborative group. The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial. Lancet. 2012;379(9834):2352–63. doi: http://dx.doi.org/10.1016/S0140-6736(12)60768-5. PubMed.

26 Grad A, Baloh RW. Vertigo of vascular origin. Clinical and electronystagmographic features in 84 cases. Arch Neurol. 1989;46(3):281–4. doi: http://dx.doi.org/10.1001/archneur.1989.00520390047014. PubMed.

27 Lee H, Cho YW. Auditory disturbance as a prodrome of anterior inferior cerebellar artery infarction. J Neurol Neurosurg Psychiatry. 2003;74(12):1644–8. doi: http://dx.doi.org/10.1136/jnnp.74.12.1644. PubMed.

28 Kim DU, Han MK, Kim JS. Isolated recurrent vertigo from stenotic posterior inferior cerebellar artery. Otol Neurotol. 2011;32(1):180–2. doi: http://dx.doi.org/10.1097/MAO.0b013e3181f6ca2f. PubMed.

29 Noh Y, Kwon OK, Kim HJ, Kim JS. Rotational vertebral artery syndrome due to compression of nondominant vertebral artery terminating in posterior inferior cerebellar artery. J Neurol. 2011;258(10):1775–80. doi: http://dx.doi.org/10.1007/s00415-011-6005-1. PubMed.

30 Choi JH, Kim MJ, Lee TH, Moon IS, Choi KD, Kim JS. Dominant vertebral artery occlusion during ipsilateral head tilt. Neurology. 2011;76(19):1679. doi: http://dx.doi.org/10.1212/WNL.0b013e318219fb6c. PubMed.

31 Rothwell PM, Giles MF, Chandratheva A, Marquardt L, Geraghty O, Redgrave JN, et al.; Early use of Existing Preventive Strategies for Stroke (EXPRESS) study. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. Lancet. 2007;370(9596):1432–42. doi: http://dx.doi.org/10.1016/S0140-6736(07)61448-2. PubMed.

32 Hankey GJ. Stroke. Lancet. 2017;389(10069):641–54. doi: http://dx.doi.org/10.1016/S0140-6736(16)30962-X. PubMed.

33 Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, et al.; Stroke Thrombolysis Trialists' Collaborative Group. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. Lancet. 2014;384(9958):1929–35. doi: http://dx.doi.org/10.1016/S0140-6736(14)60584-5. PubMed.

34 Johnston SC, Rothwell PM, Nguyen-Huynh MN, Giles MF, Elkins JS, Bernstein AL, et al. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. Lancet. 2007;369(9558):283–92. doi: http://dx.doi.org/10.1016/S0140-6736(07)60150-0. PubMed.

35 Navi BB, Kamel H, Shah MP, Grossman AW, Wong C, Poisson SN, et al. Application of the ABCD2 score to identify cerebrovascular causes of dizziness in the emergency department. Stroke. 2012;43(6):1484–9. doi: http://dx.doi.org/10.1161/STROKEAHA.111.646414. PubMed.

36 Newman-Toker DE, Kerber KA, Hsieh YH, Pula JH, Omron R, Saber Tehrani AS, et al. HINTS outperforms ABCD2 to screen for stroke in acute continuous vertigo and dizziness. Acad Emerg Med. 2013;20(10):986–96. doi: http://dx.doi.org/10.1111/acem.12223. PubMed.

37 Saber Tehrani AS, Kattah JC, Mantokoudis G, Pula JH, Nair D, Blitz A, et al. Small strokes causing severe vertigo: frequency of false-negative MRIs and nonlacunar mechanisms. Neurology. 2014;83(2):169–73. doi: http://dx.doi.org/10.1212/WNL.0000000000000573. PubMed.

38 Staab JP, Bisdorff AR, Newman-Toker DE. Vestibular Symptoms, Balance, and Their Disorders: How Will We Classify Them? Oxford, UK: Oxford University Press; 2013. Chapter 16.

39 Baloh RW, Jacobson K, Honrubia V. Horizontal semicircular canal variant of benign positional vertigo. Neurology. 1993;43(12):2542–9. doi: http://dx.doi.org/10.1212/WNL.43.12.2542. PubMed.

40 Lempert T. Horizontal benign positional vertigo. Neurology. 1994;44(11):2213–4. doi: http://dx.doi.org/10.1212/WNL.44.11.2213-a. PubMed.

41 Nuti D, Vannucchi P, Pagnini P. Benign paroxysmal positional vertigo of the horizontal canal: a form of canalolithiasis with variable clinical features. J Vestib Res. 1996;6(3):173–84. doi: http://dx.doi.org/10.1016/0957-4271(95)02040-3. PubMed.

42 Kim JS, Oh SY, Lee SH, Kang JH, Kim DU, Jeong SH, et al. Randomized clinical trial for apogeotropic horizontal canal benign paroxysmal positional vertigo. Neurology. 2012;78(3):159–66. doi: http://dx.doi.org/10.1212/WNL.0b013e31823fcd26. PubMed.

43 Kim JS, Oh SY, Lee SH, Kang JH, Kim DU, Jeong SH, et al. Randomized clinical trial for geotropic horizontal canal benign paroxysmal positional vertigo. Neurology. 2012;79(7):700–7. doi: http://dx.doi.org/10.1212/WNL.0b013e3182648b8b. PubMed.

44 Fife TD. Recognition and management of horizontal canal benign positional vertigo. Am J Otol. 1998;19(3):345–51. PubMed.

45 Baloh RW, Yue Q, Jacobson KM, Honrubia V. Persistent direction-changing positional nystagmus: another variant of benign positional nystagmus? Neurology. 1995;45(7):1297–301. doi: http://dx.doi.org/10.1212/WNL.45.7.1297. PubMed.

46 Steddin SH, Brandt T. Horizontal canal benign paroxysmal positioning vertigo (h-BPPV): transition of canalolithiasis to cupulolithiasis. Ann Neurol. 1996;40(6):918–22. doi: http://dx.doi.org/10.1002/ana.410400615. PubMed.

47 Black FO, Pesznecker SC, Homer L, Stallings V. Benign paroxysmal positional nystagmus in hospitalized subjects receiving ototoxic medications. Otol Neurotol. 2004;25(3):353–8. doi: http://dx.doi.org/10.1097/00129492-200405000-00025. PubMed.

48 Gyo K. Benign paroxysmal positional vertigo as a complication of post-operative bedrest. Laryngoscope. 1988;98(3):332–3. doi: http://dx.doi.org/10.1288/00005537-198803000-00019. PubMed.

49 Viirre E, Purcell I, Baloh RW. The Dix-Hallpike test and the canalith repositioning maneuver. Laryngoscope. 2005;115(1):184–7. doi: http://dx.doi.org/10.1097/01.mlg.0000150707.66569.d4. PubMed.

50 Zucca G, Valli S, Valli P, Perin P, Mira E. Why do benign paroxysmal positional vertigo episodes recover spontaneously? J Vestib Res. 1998;8(4):325–9. doi: http://dx.doi.org/10.1016/S0957-4271(97)00080-3. PubMed.

51 Vibert D, Kompis M, Häusler R. Benign paroxysmal positional vertigo in older women may be related to osteoporosis and osteopenia. Ann Otol Rhinol Laryngol. 2003;112(10):885–9. doi: http://dx.doi.org/10.1177/000348940311201010. PubMed.

52 Bloom J, Katsarkas A. Paroxysmal positional vertigo in the elderly. J Otolaryngol. 1989;18(3):96–8. PubMed.

53 Ishiyama A, Jacobson KM, Baloh RW. Migraine and benign positional vertigo. Ann Otol Rhinol Laryngol. 2000;109(4):377–80. doi: http://dx.doi.org/10.1177/000348940010900407. PubMed.

54 Fife TD, Iverson DJ, Lempert T, Furman JM, Baloh RW, Tusa RJ, et al.; Quality Standards Subcommittee, American Academy of Neurology. Practice parameter: therapies for benign paroxysmal positional vertigo (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2008;70(22):2067–74. doi: http://dx.doi.org/10.1212/01.wnl.0000313378.77444.ac. PubMed.

55 von Brevern M. Benign paroxysmal positional vertigo. Semin Neurol. 2013;33(3):204–11. doi: http://dx.doi.org/10.1055/s-0033-1354590. PubMed.

56 Barany R. Diagnose von Krankheitserscheinungen im Bereiche des Otolithenapparatus. Acta Otolaryngol. 1920;2(3):434–7. doi: http://dx.doi.org/10.3109/00016482009123103.

57 Epley JM. Canalith repositioning maneuver. Otolaryngol Head Neck Surg. 1994;111(5):688–89. doi: http://dx.doi.org/10.1177/019459989411100530. PubMed.

58 Semont A, Freyss G, Vitte E. Curing the BPPV with a liberatory maneuver. Adv Otorhinolaryngol. 1988;42:290–3. doi: http://dx.doi.org/10.1159/000416126. PubMed.

59 McClure JA. Horizontal canal BPV. J Otolaryngol. 1985;14(1):30–5. PubMed.

60 Casani AP, Nacci A, Dallan I, Panicucci E, Gufoni M, Sellari-Franceschini S. Horizontal semicircular canal benign paroxysmal positional vertigo: effectiveness of two different methods of treatment. Audiol Neurootol. 2011;16(3):175–84. doi: http://dx.doi.org/10.1159/000317113. PubMed.

61 Baloh RW, Yue Q, Jacobson KM, Honrubia V. Persistent direction-changing positional nystagmus: another variant of benign positional nystagmus? Neurology. 1995;45(7):1297–301. doi: http://dx.doi.org/10.1212/WNL.45.7.1297. PubMed.

62 Bertholon P, Bronstein AM, Davies RA, Rudge P, Thilo KV. Positional down beating nystagmus in 50 patients: cerebellar disorders and possible anterior semicircular canalithiasis. J Neurol Neurosurg Psychiatry. 2002;72(3):366–72. doi: http://dx.doi.org/10.1136/jnnp.72.3.366. PubMed.

63 Califano L, Salafia F, Mazzone S, Melillo MG, Califano M. Anterior canal BPPV and apogeotropic posterior canal BPPV: two rare forms of vertical canalolithiasis. Acta Otorhinolaryngol Ital. 2014;34(3):189–97. PubMed.

64 Kim YK, Shin JE, Chung JW. The effect of canalith repositioning for anterior semicircular canal canalithiasis. ORL J Otorhinolaryngol Relat Spec. 2005;67(1):56–60. doi: http://dx.doi.org/10.1159/000084336. PubMed.

65 Korres SG, Balatsouras DG. Diagnostic, pathophysiologic, and therapeutic aspects of benign paroxysmal positional vertigo. Otolaryngol Head Neck Surg. 2004;131(4):438–44. doi: http://dx.doi.org/10.1016/j.otohns.2004.02.046. PubMed.

66 Lin GC, Basura GJ, Wong HT, Heidenreich KD. Canal switch after canalith repositioning procedure for benign paroxysmal positional vertigo. Laryngoscope. 2012;122(9):2076–8. doi: http://dx.doi.org/10.1002/lary.23315. PubMed.

67 Foster CA, Zaccaro K, Strong D. Canal conversion and reentry: a risk of Dix-Hallpike during canalith repositioning procedures. Otol Neurotol. 2012;33(2):199–203. doi: http://dx.doi.org/10.1097/MAO.0b013e31823e274a. PubMed.

68 Anagnostou E, Stamboulis E, Kararizou E. Canal conversion after repositioning procedures: comparison of Semont and Epley maneuver. J Neurol. 2014;261(5):866–9. doi: http://dx.doi.org/10.1007/s00415-014-7290-2. PubMed.

69 Sharon JD, Trevino C, Schubert MC, Carey JP. Treatment of Menière's Disease. Curr Treat Options Neurol. 2015;17(4):14. doi: http://dx.doi.org/10.1007/s11940-015-0341-x. PubMed.

70 Pirodda A, Ferri GG, Raimondi MC, Borghi C. Diuretics in Meniere disease: a therapy or a potential cause of harm? Med Hypotheses. 2011;77(5):869–71. doi: http://dx.doi.org/10.1016/j.mehy.2011.07.060. PubMed.

71 Thirlwall AS, Kundu S. Diuretics for Ménière's disease or syndrome. Cochrane Database Syst Rev. 2006;(3):CD003599. PubMed.

72 Adrion C, Fischer CS, Wagner J, Gürkov R, Mansmann U, Strupp M; BEMED Study Group. Efficacy and safety of betahistine treatment in patients with Meniere's disease: primary results of a long term, multicentre, double blind, randomised, placebo controlled, dose defining trial (BEMED trial). BMJ. 2016;352:h6816. doi: http://dx.doi.org/10.1136/bmj.h6816. PubMed.

73 Bertlich M, Ihler F, Freytag S, Weiss BG, Strupp M, Canis M. Histaminergic H3-Heteroreceptors as a Potential Mediator of Betahistine-Induced Increase in Cochlear Blood Flow. Audiol Neurootol. 2015;20(5):283–93. doi: http://dx.doi.org/10.1159/000368293. PubMed.

74 Bertlich M, Ihler F, Sharaf K, Weiss BG, Strupp M, Canis M. Betahistine metabolites, aminoethylpyridine, and hydroxyethylpyridine increase cochlear blood flow in guinea pigs in vivo. Int J Audiol. 2014;53(10):753–9. doi: http://dx.doi.org/10.3109/14992027.2014.917208. PubMed.

75 Møller MN, Kirkeby S, Vikesså J, Nielsen FC, Caye-Thomasen P. Expression of histamine receptors in the human endolymphatic sac: the molecular rationale for betahistine use in Menieres disease. Eur Arch Otorhinolaryngol. 2016;273(7):1705–10. doi: http://dx.doi.org/10.1007/s00405-015-3731-5. PubMed.

76 Nauta JJ. Meta-analysis of clinical studies with betahistine in Ménière's disease and vestibular vertigo. Eur Arch Otorhinolaryngol. 2014;271(5):887–97. doi: http://dx.doi.org/10.1007/s00405-013-2596-8. PubMed.

77 Alles MJ, der Gaag MA, Stokroos RJ. Intratympanic steroid therapy for inner ear diseases, a review of the literature. Eur Arch Otorhinolaryngol. 2006;263(9):791–7. doi: http://dx.doi.org/10.1007/s00405-006-0065-3. PubMed.

78 Lambert PR, Nguyen S, Maxwell KS, Tucci DL, Lustig LR, Fletcher M, et al. A randomized, double-blind, placebo-controlled clinical study to assess safety and clinical activity of OTO-104 given as a single intratympanic injection in patients with unilateral Ménière's disease. Otol Neurotol. 2012;33(7):1257–65. doi: http://dx.doi.org/10.1097/MAO.0b013e318263d35d. PubMed.

79 Cohen-Kerem R, Kisilevsky V, Einarson TR, Kozer E, Koren G, Rutka JA. Intratympanic gentamicin for Menière's disease: a meta-analysis. Laryngoscope. 2004;114(12):2085–91. doi: http://dx.doi.org/10.1097/01.mlg.0000149439.43478.24. PubMed.

80 Ishiyama G, Lopez I, Baloh RW, Ishiyama A. Histopathology of the vestibular end organs after intratympanic gentamicin failure for Meniere's disease. Acta Otolaryngol. 2007;127(1):34–40. doi: http://dx.doi.org/10.1080/00016480600672600. PubMed.

81 Pullens B, van Benthem PP. Intratympanic gentamicin for Ménière's disease or syndrome. Cochrane Database Syst Rev. 2011;(3):CD008234. PubMed.

82 Stokroos R, Kingma H. Selective vestibular ablation by intratympanic gentamicin in patients with unilateral active Ménière's disease: a prospective, double-blind, placebo-controlled, randomized clinical trial. Acta Otolaryngol. 2004;124(2):172–5. doi: http://dx.doi.org/10.1080/00016480410016621. PubMed.

83 Watson GJ, Nelson C, Irving RM. Is low-dose intratympanic gentamicin an effective treatment for Ménière's disease: the Birmingham experience. J Laryngol Otol. 2015;129(10):970–3. doi: http://dx.doi.org/10.1017/S0022215115002200. PubMed.

84 Viana LM, Bahmad F, Jr, Rauch SD. Intratympanic gentamicin as a treatment for drop attacks in patients with Meniere's disease. Laryngoscope. 2014;124(9):2151–4. doi: http://dx.doi.org/10.1002/lary.24716. PubMed.

85 Pullens B, Verschuur HP, van Benthem PP. Surgery for Ménière's disease. Cochrane Database Syst Rev. 2013;(2):CD005395. PubMed.

86 Committee on Hearing and Equilibrium . Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Menière's disease. Otolaryngol Head Neck Surg. 1995;113(3):181–5. doi: http://dx.doi.org/10.1016/S0194-5998(95)70102-8. PubMed.

87 Postema RJ, Kingma CM, Wit HP, Albers FW, Van Der Laan BF. Intratympanic gentamicin therapy for control of vertigo in unilateral Menire's disease: a prospective, double-blind, randomized, placebo-controlled trial. Acta Otolaryngol. 2008;128(8):876–80. doi: http://dx.doi.org/10.1080/00016480701762458. PubMed.

88 Ihler F, Bertlich M, Sharaf K, Strieth S, Strupp M, Canis M. Betahistine exerts a dose-dependent effect on cochlear stria vascularis blood flow in guinea pigs in vivo. PLoS One. 2012;7(6):e39086. doi: http://dx.doi.org/10.1371/journal.pone.0039086. PubMed.

89 Strupp M, Cnyrim CD, Brandt T. Vertigo and Dizziness: Treatment of Benign Paroxysmal Positional Vertigo, Vestibular Neuritis and Menière's Disease. Evidence-based Neurology: Management of Neurological Disorders: Blackwell Publishing Ltd; 2007. pp 59–69.

90 Strupp M, Hupert D, Frenzel C, Wagner J, Hahn A, Jahn K, et al. Long-term prophylactic treatment of attacks of vertigo in Menière's disease--comparison of a high with a low dosage of betahistine in an open trial. Acta Otolaryngol. 2008;128(5):520–4. doi: http://dx.doi.org/10.1080/00016480701724912. PubMed.

91 Lezius F, Adrion C, Mansmann U, Jahn K, Strupp M. High-dosage betahistine dihydrochloride between 288 and 480 mg/day in patients with severe Menière's disease: a case series. Eur Arch Otorhinolaryngol. 2011;268(8):1237–40. doi: http://dx.doi.org/10.1007/s00405-011-1647-2. PubMed.

92 Kerber KA, Schweigler L, West BT, Fendrick AM, Morgenstern LB. Value of computed tomography scans in ED dizziness visits: analysis from a nationally representative sample. Am J Emerg Med. 2010;28(9):1030–6. doi: http://dx.doi.org/10.1016/j.ajem.2009.06.007. PubMed.

93 Garduño-Anaya MA, Couthino De Toledo H, Hinojosa-González R, Pane-Pianese C, Ríos-Castañeda LC. Dexamethasone inner ear perfusion by intratympanic injection in unilateral Ménière's disease: a two-year prospective, placebo-controlled, double-blind, randomized trial. Otolaryngol Head Neck Surg. 2005;133(2):285–94. doi: http://dx.doi.org/10.1016/j.otohns.2005.05.010. PubMed.

94 Phillips JS, Westerberg B. Intratympanic steroids for Ménière's disease or syndrome. Cochrane Database Syst Rev. 2011;(7):CD008514. PubMed.

95 Boleas-Aguirre MS, Lin FR, Della Santina CC, Minor LB, Carey JP. Longitudinal results with intratympanic dexamethasone in the treatment of Ménière's disease. Otol Neurotol. 2008;29(1):33–8. doi: http://dx.doi.org/10.1097/mao.0b013e31815dbafc. PubMed.

96 Casani AP, Piaggi P, Cerchiai N, Seccia V, Franceschini SS, Dallan I. Intratympanic treatment of intractable unilateral Meniere disease: gentamicin or dexamethasone? A randomized controlled trial. Otolaryngol Head Neck Surg. 2012;146(3):430–7. doi: http://dx.doi.org/10.1177/0194599811429432. PubMed.

97 Colletti V, Carner M, Colletti L. Auditory results after vestibular nerve section and intratympanic gentamicin for Ménière's disease. Otol Neurotol. 2007;28(2):145–51. doi: http://dx.doi.org/10.1097/MAO.0b013e31802c7989. PubMed.

98 Minor LB. Intratympanic gentamicin for control of vertigo in Meniere's disease: vestibular signs that specify completion of therapy. Am J Otol. 1999;20(2):209–19. PubMed.

99 Glasscock ME, 3rd, Thedinger BA, Cueva RA, Jackson CG. An analysis of the retrolabyrinthine vs. the retrosigmoid vestibular nerve section. Otolaryngol Head Neck Surg. 1991;104(1):88–95. doi: http://dx.doi.org/10.1177/019459989110400116. PubMed.

100 Mantokoudis G, Saber Tehrani AS, Wong AL, Agrawal Y, Wenzel A, Carey JP. Adaptation and compensation of vestibular responses following superior canal dehiscence surgery. Otol Neurotol. 2016;37(9):1399–405. doi: http://dx.doi.org/10.1097/MAO.0000000000001196. PubMed.

101 Minor LB, Solomon D, Zinreich JS, Zee DS. Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. Arch Otolaryngol Head Neck Surg. 1998;124(3):249–58. doi: http://dx.doi.org/10.1001/archotol.124.3.249. PubMed.

102 Mueller SA, Vibert D, Haeusler R, Raabe A, Caversaccio M. Surgical capping of superior semicircular canal dehiscence. Eur Arch Otorhinolaryngol. 2014;271(6):1369–74. doi: http://dx.doi.org/10.1007/s00405-013-2533-x. PubMed.

103 Amoodi HA, Makki FM, McNeil M, Bance M. Transmastoid resurfacing of superior semicircular canal dehiscence. Laryngoscope. 2011;121(5):1117–23. doi: http://dx.doi.org/10.1002/lary.21398. PubMed.

104 Agrawal SK, Parnes LS. Human experience with canal plugging. Ann N Y Acad Sci. 2001;942(1):300–5. doi: http://dx.doi.org/10.1111/j.1749-6632.2001.tb03754.x. PubMed.

105 Brandt T, Dieterich M. Vestibular paroxysmia: vascular compression of the eighth nerve? Lancet. 1994;343(8900):798–9. doi: http://dx.doi.org/10.1016/S0140-6736(94)91879-1. PubMed.

106 Hüfner K, Barresi D, Glaser M, Linn J, Adrion C, Mansmann U, et al. Vestibular paroxysmia: diagnostic features and medical treatment. Neurology. 2008;71(13):1006–14. doi: http://dx.doi.org/10.1212/01.wnl.0000326594.91291.f8. PubMed.

107 Brandt T, Dieterich M. [Vertigo caused by neurovascular compression, "vestibular paroxysm"?]. Nervenarzt. 1990;61(6):376–8. Article in German. PubMed.

108 Strupp M, von Stuckrad-Barre S, Brandt T, Tonn JC. Teaching neuroimages: Compression of the eighth cranial nerve causes vestibular paroxysmia. Neurology. 2013;80(7):e77. doi: http://dx.doi.org/10.1212/WNL.0b013e318281cc2c. PubMed.

109 Chimirri S, Aiello R, Mazzitello C, Mumoli L, Palleria C, Altomonte M, et al. Vertigo/dizziness as a Drugs' adverse reaction. J Pharmacol Pharmacother. 2013;4(5, Suppl 1):104–9. doi: http://dx.doi.org/10.4103/0976-500X.120969. PubMed.

110 Shill HA, Fife TD. Causes of imbalance and abnormal gait that may be misdiagnosed. Semin Neurol. 2013;33(3):270–5. doi: http://dx.doi.org/10.1055/s-0033-1354601. PubMed.

111 Baier B, Winkenwerder E, Dieterich M. "Vestibular migraine": effects of prophylactic therapy with various drugs. A retrospective study. J Neurol. 2009;256(3):436–42. doi: http://dx.doi.org/10.1007/s00415-009-0111-3. PubMed.

112 Dieterich M, Brandt T. Episodic vertigo related to migraine (90 cases): vestibular migraine? J Neurol. 1999;246(10):883–92. doi: http://dx.doi.org/10.1007/s004150050478. PubMed.

113 Lempert T. Vestibular migraine. Semin Neurol. 2013;33(3):212–8. doi: http://dx.doi.org/10.1055/s-0033-1354596. PubMed.

114 Neuhauser H, Radtke A, von Brevern M, Lempert T. Zolmitriptan for treatment of migrainous vertigo: a pilot randomized placebo-controlled trial. Neurology. 2003;60(5):882–3. doi: http://dx.doi.org/10.1212/01.WNL.0000049476.40047.A3. PubMed.

115 Harker LA, Rassekh CH. Episodic vertigo in basilar artery migraine. Otolaryngol Head Neck Surg. 1987;96(3):239–50. doi: http://dx.doi.org/10.1177/019459988709600303. PubMed.

116 Reploeg MD, Goebel JA. Migraine-associated dizziness: patient characteristics and management options. Otol Neurotol. 2002;23(3):364–71. doi: http://dx.doi.org/10.1097/00129492-200205000-00024. PubMed.

117 Baloh RW, Foster CA, Yue Q, Nelson SF. Familial migraine with vertigo and essential tremor. Neurology. 1996;46(2):458–60. doi: http://dx.doi.org/10.1212/WNL.46.2.458. PubMed.

118 Newman-Toker DE, Dy FJ, Stanton VA, Zee DS, Calkins H, Robinson KA. How often is dizziness from primary cardiovascular disease true vertigo? A systematic review. J Gen Intern Med. 2008;23(12):2087–94. doi: http://dx.doi.org/10.1007/s11606-008-0801-z. PubMed.

119 Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, et al.; American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Epidemiology and Prevention; Council for High Blood Pressure Research; Council on Peripheral Vascular Disease, and Interdisciplinary Council on Quality of Care and Outcomes Research. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011;42(2):517–84. doi: http://dx.doi.org/10.1161/STR.0b013e3181fcb238. PubMed.

120 Ophoff RA, Terwindt GM, Vergouwe MN, van Eijk R, Oefner PJ, Hoffman SM, et al. Familial hemiplegic migraine and episodic ataxia type-2 are caused by mutations in the Ca2+ channel gene CACNL1A4. Cell. 1996;87(3):543–52. doi: http://dx.doi.org/10.1016/S0092-8674(00)81373-2. PubMed.

121 Jen J, Kim GW, Baloh RW. Clinical spectrum of episodic ataxia type 2. Neurology. 2004;62(1):17–22. doi: http://dx.doi.org/10.1212/01.WNL.0000101675.61074.50. PubMed.

122 Strupp M, Kalla R, Dichgans M, Freilinger T, Glasauer S, Brandt T. Treatment of episodic ataxia type 2 with the potassium channel blocker 4-aminopyridine. Neurology. 2004;62(9):1623–5. doi: http://dx.doi.org/10.1212/01.WNL.0000125691.74109.53. PubMed.

123 Strupp M, Kalla R, Claassen J, Adrion C, Mansmann U, Klopstock T, et al. A randomized trial of 4-aminopyridine in EA2 and related familial episodic ataxias. Neurology. 2011;77(3):269–75. doi: http://dx.doi.org/10.1212/WNL.0b013e318225ab07. PubMed.

124 Claassen J, Teufel J, Kalla R, Spiegel R, Strupp M. Effects of dalfampridine on attacks in patients with episodic ataxia type 2: an observational study. J Neurol. 2013;260(2):668–9. doi: http://dx.doi.org/10.1007/s00415-012-6764-3. PubMed.

125 Staab JP, Balaban CD, Furman JM. Threat assessment and locomotion: clinical applications of an integrated model of anxiety and postural control. Semin Neurol. 2013;33(3):297–306. doi: http://dx.doi.org/10.1055/s-0033-1356462. PubMed.

126 Horii A, Kitahara T, Masumura C, et al. Effects of milnacipran, a serotonin noradrenaline reuptake inhibitor (SNRI) on subjective handicaps and posturography in dizzy patients. Abstract presented at the XXVth Congress of the Barany Society. Kyoto, Japan. March 31 – April 3, 2008.

127 Hain TC, Cherchi M, Yacovino DA. Bilateral vestibular loss. Semin Neurol. 2013;33(3):195–203. doi: http://dx.doi.org/10.1055/s-0033-1354597. PubMed.

128 Selimoglu E. Aminoglycoside-induced ototoxicity. Curr Pharm Des. 2007;13(1):119–26. doi: http://dx.doi.org/10.2174/138161207779313731. PubMed.

129 Schaefer SD, Wright CG, Post JD, Frenkel EP. Cis-platinum vestibular toxicity. Cancer. 1981;47(5):857–9. doi: http://dx.doi.org/10.1002/1097-0142(19810301)47:5<857::AID-CN-CR2820470508>3.0.CO;2-M. PubMed.

130 Migliori G, Battisti E, Pari M, Vitelli N, Cingolani C. A shifty diagnosis: Cogan's syndrome. A case report and review of the literature. Acta Otorhinolaryngol Ital. 2009;29(2):108–13. PubMed.

131 Ogata Y, Sekitani T, Shimogori H, Ikeda T. Bilateral vestibular neuronitis. Acta Otolaryngol Suppl. 1993;113(sup503):57–60. doi: http://dx.doi.org/10.3109/00016489309128073. PubMed.

132 Schuknecht HF, Witt RL. Acute bilateral sequential vestibular neuritis. Am J Otolaryngol. 1985;6(4):255–7. doi: http://dx.doi.org/10.1016/S0196-0709(85)80051-X. PubMed.

133 Nabi S, Parnes LS. Bilateral Ménière's disease. Curr Opin Otolaryngol Head Neck Surg. 2009;17(5):356–62. doi: http://dx.doi.org/10.1097/MOO.0b013e3283304cb3. PubMed.

134 Kobayashi H, Mizukoshi K, Watanabe Y, Nagasaki T, Ito M, Aso S. Otoneurological findings in inner ear syphilis. Acta Otolaryngol Suppl. 1991;111(suppl 481):551–5. doi: http://dx.doi.org/10.3109/00016489109131468. PubMed.

135 Durham JS, Longridge NS, Smith JM, Jones H. Clinical manifestations of otological syphilis. J Otolaryngol. 1984;13(3):175–9. PubMed.

136 Colvin IB. Audiovestibular manifestations of sarcoidosis: a review of the literature. Laryngoscope. 2006;116(1):75–82. doi: http://dx.doi.org/10.1097/01.mlg.0000184580.52723.9f. PubMed.

137 Feneley MR, Murthy P. Acute bilateral vestibulo-cochlear dysfunction following occipital fracture. J Laryngol Otol. 1994;108(1):54–6. doi: http://dx.doi.org/10.1017/S0022215100125836. PubMed.

138 Benitez JT, Bouchard KR, Lane-Szopo D. Pathology of deafness and disequilibrium in head injury:a human temporal bone study. Am J Otol. 1980;1(3):163–7. PubMed.

139 Demer JL, Honrubia V, Baloh RW. Dynamic visual acuity: a test for oscillopsia and vestibulo-ocular reflex function. Am J Otol. 1994;15(3):340–7. PubMed.

140 Longridge NS, Mallinson AI. A discussion of the dynamic illegible "E" test: a new method of screening for aminoglycoside vestibulotoxicity. Otolaryngol Head Neck Surg. 1984;92(6):671–7. doi: http://dx.doi.org/10.1177/019459988409200614. PubMed.

141 Staecker H, Praetorius M, Baker K, Brough DE. Vestibular hair cell regeneration and restoration of balance function induced by math1 gene transfer. Otol Neurotol. 2007;28(2):223–31. doi: http://dx.doi.org/10.1097/MAO.0b013e31802b3225. PubMed.

142 Porciuncula F, Johnson CC, Glickman LB. The effect of vestibular rehabilitation on adults with bilateral vestibular hypofunction: a systematic review. J Vestib Res. 2012;22(5-6):283–98. PubMed.

143 Spiegel R, Kalla R, Rettinger N, Schneider E, Straumann D, Marti S, et al. Head position during resting modifies spontaneous daytime decrease of downbeat nystagmus. Neurology. 2010;75(21):1928–32. doi: http://dx.doi.org/10.1212/WNL.0b013e3181feb22f. PubMed.

144 Wagner JN, Glaser M, Brandt T, Strupp M. Downbeat nystagmus: aetiology and comorbidity in 117 patients. J Neurol Neurosurg Psychiatry. 2008;79(6):672–7. doi: http://dx.doi.org/10.1136/jnnp.2007.126284. PubMed.

145 Kalla R, Glasauer S, Büttner U, Brandt T, Strupp M. 4-aminopyridine restores vertical and horizontal neural integrator function in downbeat nystagmus. Brain. 2007;130(9):2441–51. doi: http://dx.doi.org/10.1093/brain/awm172. PubMed.

146 Kalla R, Spiegel R, Claassen J, Bardins S, Hahn A, Schneider E, et al. Comparison of 10-mg doses of 4-aminopyridine and 3,4-diaminopyridine for the treatment of downbeat nystagmus. J Neuroophthalmol. 2011;31(4):320–5. doi: http://dx.doi.org/10.1097/WNO.0b013e3182258086. PubMed.

147 Claassen J, Spiegel R, Kalla R, Faldon M, Kennard C, Danchaivijitr C, et al. A randomised double-blind, cross-over trial of 4-aminopyridine for downbeat nystagmus--effects on slowphase eye velocity, postural stability, locomotion and symptoms. J Neurol Neurosurg Psychiatry. 2013;84(12):1392–9. doi: http://dx.doi.org/10.1136/jnnp-2012-304736. PubMed.

148 Glasauer S, Kalla R, Büttner U, Strupp M, Brandt T. 4-aminopyridine restores visual ocular motor function in upbeat nystagmus. J Neurol Neurosurg Psychiatry. 2005;76(3):451–3. doi: http://dx.doi.org/10.1136/jnnp.2004.045716. PubMed.

149 Strupp M, Schüler O, Krafczyk S, Jahn K, Schautzer F, Büttner U, et al. Treatment of downbeat nystagmus with 3,4-diaminopyridine: a placebo-controlled study. Neurology. 2003;61(2):165–70. doi: http://dx.doi.org/10.1212/01.WNL.0000078893.41040.56. PubMed.

150 Currie JN, Matsuo V. The use of clonazepam in the treatment of nystagmus-induced oscillopsia. Ophthalmology. 1986;93(7):924–32. doi: http://dx.doi.org/10.1016/S0161-6420(86)33640-6. PubMed.

151 Young YH, Huang TW. Role of clonazepam in the treatment of idiopathic downbeat nystagmus. Laryngoscope. 2001;111(8):1490–3. doi: http://dx.doi.org/10.1097/00005537-200108000-00029. PubMed.

152 Mehta AR, Kennard C. The pharmacological treatment of acquired nystagmus. Pract Neurol. 2012;12(3):147–53. doi: http://dx.doi.org/10.1136/practneurol-2011-000181. PubMed.

153 Spiegel R, Rettinger N, Kalla R, Lehnen N, Straumann D, Brandt T, et al. The intensity of downbeat nystagmus during daytime. Ann N Y Acad Sci. 2009;1164(1):293–9. doi: http://dx.doi.org/10.1111/j.1749-6632.2009.03865.x. PubMed.

154 Spiegel R, Claassen J, Teufel J, Bardins S, Schneider E, Lehrer Rettinger N, et al. Resting in darkness improves downbeat nystagmus: evidence from an observational study. Ann N Y Acad Sci. 2016;1375(1):66–73. doi: http://dx.doi.org/10.1111/nyas.13172. PubMed.

155 Franko Zeitz P, Hegemann S. Auge, Sehen und Schwindel [The eye, vision and vertigo]. HNO. 2013;61(9):772–6. Article in German. doi: http://dx.doi.org/10.1007/s00106-013-2743-y. PubMed.

156 Wrisley DM, Sparto PJ, Whitney SL, Furman JM. Cervicogenic dizziness: a review of diagnosis and treatment. J Orthop Sports Phys Ther. 2000;30(12):755–66. doi: http://dx.doi.org/10.2519/jospt.2000.30.12.755. PubMed.

157 Fife TD, Giza C. Posttraumatic vertigo and dizziness. Semin Neurol. 2013;33(3):238–43. doi: http://dx.doi.org/10.1055/s-0033-1354599. PubMed.

158 Brandt T, Strupp M, Dieterich M. Vestibular paroxysmia: a treatable neurovascular cross-compression syndrome. J Neurol. 2016;263(S1, Suppl 1):90–6. doi: http://dx.doi.org/10.1007/s00415-015-7973-3. PubMed.